An atlas of transcriptional, chromatin accessibility, and surface marker changes in human mesoderm development.

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Public Summary:
Mesoderm is the developmental precursor to myriad human tissues including bone, heart, and skeletal muscle. Unravelling the molecular events through which these lineages become diversified from one another is integral to developmental biology and understanding changes in cellular fate. To this end, we developed an in vitro system to differentiate human pluripotent stem cells through primitive streak intermediates into paraxial mesoderm and its derivatives (somites, sclerotome, dermomyotome) and separately, into lateral mesoderm and its derivatives (cardiac mesoderm). Whole-population and single-cell analyses of these purified populations of human mesoderm lineages through RNA-seq, ATAC-seq, and high-throughput surface marker screens illustrated how transcriptional changes co-occur with changes in open chromatin and surface marker landscapes throughout human mesoderm development. This molecular atlas will facilitate study of human mesoderm development (which cannot be interrogated in vivo due to restrictions on human embryo studies) and provides a broad resource for the study of gene regulation in development at the single-cell level, knowledge that might one day be exploited for regenerative medicine.

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